

# QUARTERLY SUMMARY

## OF THE

# IMPROVEMENTS AND DISCOVERIES

## IN THE

# MEDICAL SCIENCES.

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### ANATOMY AND PHYSIOLOGY.

1. *Experiments on some of the Various Circumstances Influencing Cutaneous Absorption.* By AUGUSTUS WALLER, M. D., Prof. Phys. in Queen's Coll., Birmingham.—In some former experiments<sup>1</sup> I endeavoured to elucidate the phenomena of cutaneous absorption on the lower animals (batracia), by immersing the hinder extremities in various solutions, and afterwards watching the period at which the absorbed substances reached the tongue, where their presence was detected by means of some reagent applied to its surface: as, for instance, a salt of iron, when the legs were immersed in a solution of yellow ferrocyanide of potassium; Prussian blue was then formed as soon as the ferrocyanide was brought to the tongue.

Furthermore, I was able to detect, by the aid of the microscope, the "lieux d'élection," or preference spots, where the cyanide escaped from the vessels.

On the present occasion I shall endeavour to elucidate cutaneous absorption on the higher animals, and, if possible, to give a more definite view of this function, by determining, by accurate measurement, the degree of rapidity, the peculiarities, &c., which it may offer in various conditions.

A very simple mode of demonstrating the existence of cutaneous absorption is by immersing the leg of a young guinea pig, not more than half-grown, into a mixture of equal parts of chloroform and tincture of aconite. After fifteen minutes' immersion, the part will be found insensible at the surface and extremities, and, after a short time, symptoms of poisoning by aconite will supervene, viz., nausea, efforts at vomiting, sometimes vomiting of bile, coldness of the surface and extremities, circulation very weak, laborious respiration, slight convulsive symptoms, and death.

The influence of age, or of thickening of the cuticle, is easily seen in the same way; for, if instead of a young animal we take an adult one, we obtain no poisoning, but merely local insensibility and slight disturbance of respiration, &c.

Another not less instructive experiment consists in replacing the mixture of chloroform and tincture of aconite by simple tincture of aconite. In this case, the limb may be indefinitely immersed without our obtaining either local insensibility or death, or indeed any symptom whatever of the presence of aconite in the system.

A fourth experiment, which consists in dividing the sciatic nerve, shows the influence of innervation on the function of absorption; for, if performed on an adult animal, and consequently one incapable of absorbing aconite in quantity

<sup>1</sup> Waller, "Absorption of various Substances through the Skin of the Frog."—*Frorieps Tagesberichte*, 1851.

sufficient to cause death, the powers of absorption will be generally found so much augmented that the animal will be poisoned by immersion of the limb in simple tincture of aconite.

In this experiment I attribute the acceleration in the entaneous absorption to the paralysis of the bloodvessels, as in my experiments on the sympathetic nerve, where I showed that in bloodvessels the passage of the blood is completely regulated by nerves springing from the spinal cord. When the vascular nerves are paralyzed, the artery becomes greatly distended, and the blood flows faster within it. The foot after the section of the sciatic is, on this account, more hot and red; and for the same reasons it is easy to account for the more rapid absorption of medicinal agents.

A fifth experiment consists in placing a ligature on the limb, in order to impede the powers of absorption of the animal. Although the ligature does produce this result, I was rather surprised to find how much less efficient it was than is generally represented; for, whenever the least symptoms of a toxic influence made their appearance, a ligature placed over the limb rarely succeeded in saving the animal.

In order to obtain results more susceptible of measurement, I proceeded to substitute atropia for aconite, and to make use of the albino rat in lieu of the guinea pig. By this means, I possessed an agent whose intervention was immediately detected by its action on the iris. My choice of the albino rat was for the like reason, *i. e.* the facility which it offered for exact and easy measurement, in which respect this animal is far preferable to any other with which I am acquainted, unless we except the white mouse, which, however, is so liable to die from slight causes, that it is little adapted for most physiological experiments.

The *modus operandi* which I generally adopt is to immerse the limb into a small two-drachm bottle containing sufficient of the mixture to cover the foot and part of the leg. The strength of the solution of atropia being generally that from half a grain to one drachm of some menstruum, such as chloroform, alcohol, &c., I generally prefer simply to hold the animal during the experiment to any other mode of restraint. By these means I am able to guard against several causes of error, such as the direct contact of the solution with the eye or mouth, and, at the same time, avoid any unnecessary discomfort to the animal.

*Chloroform and Atropia.*—A solution of atropia in chloroform will generally be found to cause dilatation of the pupil after the foot has been immersed from two to five minutes. The dilatation, having once commenced, is usually very rapid, and the pupil very soon attains double or treble its normal diameter, which is about one-fourth to one-half a millimetre during daytime. It is easy to recognize that this dilatation is not in very simple ratio to the time occupied in its expansion, the expansion of the pupil being more nearly in proportion to the square of the time occupied than in a simple arithmetical ratio. Immersion of one limb causes both pupils to dilate equally, except in some few instances, where one pupil expands much more than the other, from some constitutional peculiarity, which remains the same whichever foot be immersed.

Although I have never failed to obtain dilatation of the pupils by the immersion of the foot in this solution of atropia, yet, in some cases, it takes more slowly than in others. The age of the animal has, in this respect, a most marked retarding influence. On animals only about a third grown, it will often occur at about two and a half minutes after immersion, while in the adult it generally requires five minutes and upwards.

The local effects of immersion are redness, heat, and swelling of the foot, accompanied sometimes with extravasation from some smaller vessels, when the immersion has been prolonged for ten minutes and upwards. The sensibility of the part is likewise diminished, but in no case so as to produce insensibility. The amount of irritation is of course variable, according to the duration of the immersion. It is, however, important to remark that full dilatation of the pupils may be obtained without any symptoms beyond those of a temporary active vascularization of the part, which quickly disappears when the irritating cause is removed, and which presents no more active symptoms than those produced by neuro-paralysis of the vessels after section of the sciatic nerve.

If instead of immersing the limb as above, we merely plunge it for a moment in the solution, we likewise may have dilatation of the pupil, but more slowly.

The same effects are obtained even although the limb be washed on its withdrawal from the solution, which would lead to the inference that the effect in that case is owing to absorption of the atropia, at all events beneath the cuticle.

In the case of a solution of atropia in turpentine, a still more curious effect is observed, viz., that during immersion in the liquid the pupil scarcely, if at all, dilates; whereas, immediately after the removal of the limb, the dilatation commences. Dilatation of the pupils will generally persist from twenty-four to thirty-six hours, and the return to the normal size is very gradual. In some cases the pupil may be affected after an immersion of nine minutes, the dilatation reaching three millimetres; while in others, only a very slight influence is obtained on the pupil after an immersion of from twelve to fifteen minutes. If the limb is then removed from the solution, the pupil dilates to its maximum in a few minutes. After two or three minutes' immersion, the animal shows signs of considerable pain. Much inflammation of the part follows the action of this solution, which is followed by œdema.

When we immerse the tail of the animal instead of its foot, absorption takes place much more slowly, dilatation of the pupil being produced only after the lapse of about twenty minutes.

*Atropia and Alcohol.*—If we substitute alcohol instead of chloroform as a solvent, we find that absorption is extremely slow. Instead of obtaining dilatation of the pupils in two or three minutes, we find that an immersion of twenty to thirty minutes in the alcoholic solution will only produce very slight effects. At the same time the local irritation is much less than that caused by chloroform. Alcohol of various strength, from proof spirits upwards, had the same result as a solvent.

*Atropia in Water, with the addition of sufficient Acetic Acid for its solution.*—The absorption of atropia in this state is very slow, thirty minutes' immersion frequently producing no dilatation of the pupils. Dilatation is then promoted by removal of the limb from the solution.

*Watery Extract of Belladonna.*—When rubbed over the leg and tail, this substance was not found, after the lapse of an hour, to produce any dilatation of the pupil.

Tincture of belladonna, with half its quantity of chloroform, produced dilatation at the end of fifteen minutes. The part was found on removal to be completely insensible, and considerably swollen from œdema, which lasted for several days.

Atropia with strong alcohol and ammonia produced dilatation of the pupil after twenty-five minutes' immersion. In this case, the ammonia was added for the purpose of ascertaining how far irritation of the part was conducive to absorption. Slight vesication was the consequence of the presence of ammonia. The acceleration of the absorption was very slight, as the solution produced no dilatation until after twenty-four minutes' immersion.

*Absorption of Morphia.*—The foot of a young rat at one-third its growth was immersed in a solution consisting of half a grain of acetate of morphia in twenty drops of alcohol and one drachm of chloroform. In five minutes the pupils gradually dilated to the maximum; the limb was then withdrawn; foot hot, red, and rather swollen. Irritation of the skin caused no cry, the animal merely withdrawing the part. Somnolency existed, from which any noise aroused it, but only for a moment. When placed on its back, the animal remained in that position. Respiration accelerated. Vision when roused very imperfect, as was shown by its falling off the table. The pupils continued fully dilated, the iris being reduced to an almost imperceptible circle, the dilatation exceeding that which I have been able to attain even with atropia. I will not dwell more fully at present on this last interesting fact, which is opposed to what we generally meet with in the administration of morphia. Twelve hours after, pupils normal, animal quite well.

*Strychnia and Chloroform.*—After three minutes' immersion of foot, dilatation of pupils ensued. After five minutes, the immersed limb was very sensitive, apparently more so than normal. Limb removed from solution: spasms about

the throat now appeared, which were rapidly succeeded by stiffness of the trunk, increasing into tetanic spasms. Death two minutes after removal.

*Strychnia and Alcohol.*—Foot immersed in a solution of alcohol and strychnia for upwards of thirty-five minutes; no symptoms of strychnine poisoning. Removed from solution and washed. Twelve hours later, no dilatation nor contraction of pupils.

The above observations evidently show that medicinal substances may be very rapidly absorbed into the circulation under certain circumstances, among which, the most important is the choice of the menstruum in which they are dissolved.

It remains for us to examine into the effect of temperature, inflammation, neuro-vascular paralysis, &c., on absorption. But, what is of still more importance, we have to see how far these facts are applicable to man in health and disease.

Meanwhile, I take this opportunity to state that a remarkable uniformity exists between cutaneous absorption in man and in the lower animals, and I believe that the application of these facts to practical medicine promises to be very important and extensive.—*Journal of the Royal Society.*

2. *Subarachnoid Fluid.*—M. JOBERT DE LAMBALLE publishes the following singular case, to prove that Magendie erroneously considered the loss of the subarachnoid fluid a cause of functional disturbance to the cerebro-spinal system.

A person of strong constitution, who was admitted into the Hôtel Dieu on the 11th of December, 1858, and died eleven days later, on the 22d, had been stabbed with a dagger by a man who was in the habit of paying her frequent visits. The blow was struck with great violence, and the blade had broken off, close to the handle of the poniard, the base corresponding to the skin, while its point penetrated into the vertebral cavity. The large bloodvessels had escaped injury, and the hemorrhage was therefore unimportant; but a continuous discharge of a serous fluid, analogous to the serum of blood, was observed oozing from the oblique wound of the integument. The sheets and bedding were wet through, so great was the amount which exuded daily, and the fluid, on examination, was found to consist of serum containing a few blood-corpuscles. It was impossible to remove the foreign body before the third day of the patient's sojourn in the hospital, and when it was withdrawn, a considerable rush of the same liquid took place. No muscular collapse, or diminution of muscular contractility was observed at any time, notwithstanding the escape of the cerebro-spinal fluid, nor any change in the mental powers. The patient having died from spinal meningitis, a post-mortem examination showed that the body of the sixth and seventh cervical vertebrae had been grazed by the instrument, the inter-vertebral substance injured, and the parietal dura mater and arachnoid perforated by the point of the blade.

The case is favourable to M. Longet's view, who, repeating Magendie's experiments, demonstrated that the withdrawal of the cerebro-spinal fluid does not materially affect the gait of animals.—*Journal of Pract. Med. and Surg.*

3. *Presence of Urea in Chyle and Lymph.*—Two years ago, M. AD. WURTZ finding at Alfort a carnivorous bull in which a fistula of the thoracic duct had been established, it occurred to him to search for urea in the chyle of this animal. To this inquiry he was induced by the consideration, that urea ought to originate, not in the capillary bloodvessels, as has been sometimes pretended, but in the intimate structure of all the tissues, at every part where materials which have become unfit for life require to be removed by the respiratory combustion. If this be the case, we ought to detect urea not only in the blood, where its presence has been ascertained for a long time past, but also in lymph, and, consequently, in the chyle of the thoracic duct. It appears, indeed, natural, that the lymphatics should contribute their share towards the absorption of the materials proceeding from the metamorphoses of the tissues, in which the radicles of these vessels are distributed. The chyle of the bull referred to was accordingly found very rich in urea. M. Wurtz coagulated, at a warm temperature, about 600 grammes of the chyle, evaporated the filtered liquid, treated it with absolute